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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,328	01/10/2008	**Abdul Waseh Basit**	33327.001	9321

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EXAMINER	
SHOMER, ISAAC	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
05/07/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket-ip@dewittross.com

Office Action Summary	Application No.	Applicant(s)	
	10/597,328	BASIT ET AL.	
	Examiner	Art Unit	
	ISAAC SHOMER	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,4-6,8,10-17 and 20-25* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☒ Claim(s) *14 and 20-25* is/are allowed.

7)☒ Claim(s) *1,4,8,10-13 and 15-17* is/are rejected.

8)☒ Claim(s) *5 and 6* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 12 March 2012, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

Claims 5 and 6 are objected to because of the following informalities: Claims 5 and 6 depend upon claim 3 which has been canceled. Applicant should amend claims 5 and 6 such that they do not depend upon a canceled claim.

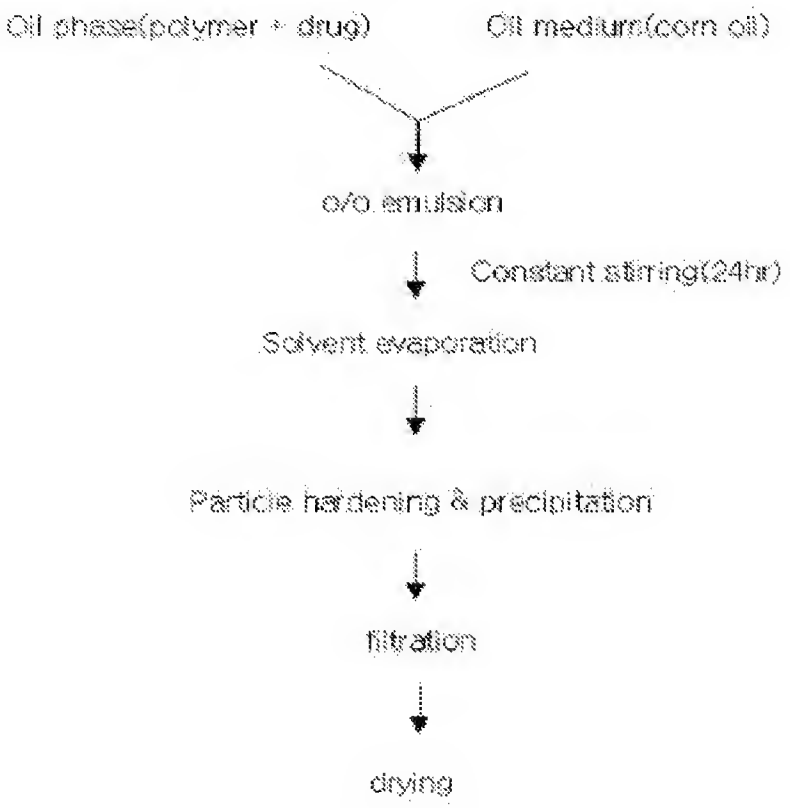
Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, 8, 10-13, 15, and 17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Journal of Microencapsulation, 2002, Vol. 19, No. 6, pages 811-822) in view of Hassan (US 2002/0119916).

Kim et al. (hereafter referred to as Kim) teaches microspheres comprising the felodipine (a drug) which were prepared by an oil/oil emulsion evaporation method, as of Kim, page 811, abstract. In one embodiment, Eudragit RL and Eudragit RS (methacrylate copolymers as required by claims 1, 11, and 12) were dissolved in an

acetonitrile/dichloromethane mixture then emulsified into corn oil using 2% Span 80 (polysorbate 80) as the surfactant, as of Kim, page 813, top two paragraphs, and page 1, Figure 1, reproduced below.



In the method of Kim, the particles made from said method are sized from 9.5 to 13.2 microns, as of Kim, page 811, abstract. Kim, when reviewing the prior art, teaches that systems comprising Eudragits are useful for the preparation dosage forms for oral administration, as of Kim, page 812, second full paragraph.

Kim does not teach “at least two surfactants”, as required by claim 1.

Hassan is drawn to a process of manufacture of particles for the delivery of water insoluble drugs, as of Hassan, abstract, wherein said process is an emulsion process. Hassan utilizes surfactants which may have a HLB value from 1 to 20, as of Hassan,

paragraph 0019. Hassan suggests polyoxyethylene sorbitan fatty acids generically, which are known by Hassan as "Spans," as of Hassan, paragraph 0027. Sorbitan sesquioleate is a preferred surfactant of Hassan, as of paragraph 0027, and the surfactant known by the trade name Arlacel 83 is suggested, as of Hassan, paragraph 0038, wherein the term Arlacel 83 is a trade name for sorbitan sesquiolate. The particles made by the method of Hassan are taught for oral administration, as of Hassan, page 5 claim 21.

It would have been prima facie obvious for one of ordinary skill in the art to have substituted the surfactants of Hassan for those of Kim. This is because the surfactants of Hassan are predictably known to be useful in an emulsion for oral administration with a reasonable expectation of success, wherein oral delivery suggested by Kim. The simple substitution of one known element (sorbitan sesquiolate, of Hassan) for another (Span 80, of Kim), to achieve predictable results (making an emulsion for oral administration) is prima facie obvious. See MPEP 2143, Exemplary Rationale B. Furthermore, Hassan teaches the entire genus of surfactants known by the trade name "span" (which includes the surfactant Span 80 of Kim), yet teaches that sorbitan sesquioleate is preferred, as of Hassan, paragraph 0027, which would have provided the skilled artisan with even greater motivation to have used sorbitan sesquiolate.

As to claim 1, Arlacel 83, as taught by Hassan, paragraph 0038, reads on the requirement of claim 1 of “at least two surfactants” as it is a combination of sorbitan monoleate and sorbitan dioleate, as of page 6 lines 6-7 of the instant specification.

Furthermore, the term Arlacel 83 is also known as sorbitan sesquiolate, as of page 7 line 7 of the specification and Hassan, paragraph 0038.

As to claim 4, Arlacel 83, being sorbitan sesquioleate, has a HLB value of 3.7, as evidenced by page 12, line 20 of the instant specification.

As to claim 8, 10, and 11, the above references do not specifically teach pH dependent release, as required by claim 8. However, the skilled artisan would have understood that the polymers used by Kim and Hassan, specifically the polymer known by the trade name Eudragit RS (as of Kim, abstract), would have possessed this property. The polymer known by the trade name "Eudragit RS" is Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.1, which is recited by claim 11, and is disclosed by the specification at page 5 line 6. As such, the polymer known as Eudragit RS, which was used in the prior art, would have had the same properties.

As to claim 12, Kim also teaches Eudragit RL, as of Kim, page 812, bottom paragraph. This is Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonioethyl methacrylate chloride) 1:2:0.2. As such, Kim does not teach the polymer known as Eudragit RS alone.

As to claim 13, Hassan teaches various drugs including prednisone, as of Hassan, paragraph 0012.

As to claim 15, Kim teaches addition of the surfactant into the corn oil phase (i.e. non-solvent continuous phase). As such, the skilled artisan would have added both surfactants of Hassan to the continuous phase.

As to claim 17, Kim teaches neither heating nor cooling, as of Kim, page 813, top two paragraphs. As such, it is understood that the emulsification occurs at room temperature, which is within the range of 10-30 degrees Celsius, as required by claim 17.

Response to Arguments:

A) In applicant's arguments dated 12 March 2012, (hereafter referred to as applicant's arguments), applicant contends that the examiner has cited Kim's teachings regarding acetonitrile being polar, water-miscible, and oil-immiscible, as of applicant's arguments, page 6, first paragraph in "Rejection of claims 1..." section.

This is not persuasive. Kim teaches that Eudragit RL and Eudragit RS (methacrylate copolymers as required by claims 1, 11, and 12) were dissolved in an acetonitrile/dichloromethane mixture then emulsified into corn oil using 2% Span 80 (polysorbate 80) as the surfactant, as of Kim, page 813, top two paragraphs, and page 1, Figure 1.

B) Applicant contends that a surfactant that is taught for use in the water-in-oil emulsions of Hassan would not have worked in the oil-in-oil emulsion system of Kim, as of applicant's arguments, page 6, bottom paragraph.

This is not persuasive. Hassan teaches the entire genus of surfactants known by the trade name "span," as of Hassan, paragraph 0020. The surfactant of Kim is Span 80, which is in the genus of spans. As such, the skilled artisan would have understood that the surfactants that are effective for the water-containing emulsion of Hassan would also have been effective for the oil-in-oil emulsions of Kim, and that there no bright line

rule that separates surfactants uses in oil-in-oil emulsions from surfactants used in water-containing emulsions.

Arguments Pertaining to Unexpected Results:

C) In applicant's arguments, page 7, top two full paragraphs, applicant contends that Examples 3 and 4 of the specification show data for the production of particles using the following surfactant systems, which have a HLB of 3.7.

- An equimolar mixture of sorbitan monoleate and sorbitan dioleate (Arlacel 83). Data for this is present in Figures 3A-3C, and 5-7.
- A mixture of 14.4% Tween 80 and 85.6% Span 86. Data is presented in Figure 4A.
- A mixture of 56.6% Span 80 and 43.5% Span 85. Data is presented in Figure 4B.

Applicant also contends that data is shown for the following mixtures, as of Example 16 of the specification, wherein these mixtures have varying HLB values:

- A mixture of 50% Span 80 and 50% Span 85 (HLB 3).
- A mixture of 53% Span 85 and 47% Span 20 (HLB 5).
- A mixture of 60% Span 80 and 40% Span 20 (HLB 6)
- A mixture of 35% Span 80 and 65% Span 20 (HLB 7).

Applicant's position appears to be that the above-cited surfactants produced desired results, whereas the use of single surfactants did not produce desired results. Applicant cites Examples 1 and 2 on pages 11-12 of the specification in support of the undesired results produced by the use of a single surfactant.

The data shown from Examples 3 and 4 do appear to show that particles produced with two different surfactants at HLB 3.7 result in a particle that is nonaggregated, whereas the use of a single surfactant results in the formation of aggregated particles, as of Figures 1 and 2. This result appears to be unexpected.

However, a review of the instant drawings does not appear to show electron micrographs of the desired examples mentioned in bullet points above for the compositions made by the method of Example 16. As such, the particles made from the methods of Example 16 are not probative of non-obviousness.

The data shown by applicant is only for surfactants with a HLB value of 3.7, and cannot necessarily be extrapolated outside that range. As no data appears to have been provided regarding compositions with surfactants with HLB values other than 3.7, the data provided by applicant is not commensurate in scope with the claimed invention.

D) In applicant's arguments, page 7, bottom paragraph, and top of paragraph on page 8, applicant contends that the choice of solvent has little effect on the morphology of the microparticles, showing that the surfactant is more crucial than the choice of solvent, citing page 15 of the specification. The examiner notes Figures 6A-6E, 7A-7C, and 8A-8H, noting that the specific combinations of acetone, methanol, and ethanol that were tested appear to result in a particle with a desirable morphology. This result appears to be unexpected. However, the data shown by applicant is only limited to specific combinations of acetone, methanol, and ethanol. As claim 1 does not recite a specific solvent, the data presented by applicant is not commensurate in scope with the claimed invention. These solvents are not reasonably representative of solvents in

general because they are all of medium polarity; they are not highly polar like water, and they are not highly non-polar like dichloromethane and diethyl ether. For example, ethanol is miscible with both water and dichloromethane, whereas water and dichloromethane are not miscible with each other. As such, the properties of ethanol, methanol, and acetone, especially with regard to miscibility and emulsion formation, would not have been shared with water, or with nonpolar solvents.

Claim 16 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Journal of Microencapsulation, 2002, Vol. 19, No. 6, pages 811-822) in view of Hassan (US 2002/0119916) as applied to claims 1, 4, 8, 10-13, 15, and 17 above, and further in view of Satturwar et al. (Journal of Microencapsulation, Vol. 19, No. 4, 2002, pages 407-413).

In applicant's arguments, page 8, bottom paragraphs, applicant contends that the teachings of Satturwar do not address the shortcomings of Kim and Hassan. This is not persuasive. As there are no shortcomings regarding the rejection over Kim and Hassan, and as no further arguments were provided regarding claim 16, this rejection is maintained.

Allowable Subject Matter

Claims 5, 6, and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. These claims are allowable

because they specifically limit the surfactant system to only those surfactants that produce particles with the unexpectedly desired morphologies, and which are commensurate in scope with applicant's showings.

Claims 14, and 23-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and claim 21 is allowable. These claims limit the solvent system to ethanol and a mixture of acetone and either ethanol or methanol. These results are commensurate in scope with the unexpected results provided by applicant, given that the unexpected results show the formation of a microparticle with the desired properties when the claimed solvents are used. Furthermore, there is no prima facie case of obviousness set forth regarding the use of this solvent system. There would have been no reason to have substituted the acetonitrile/dichloromethane solvent system, which include no protic hydrogen atoms, for a solvent system requiring ethanol or methanol, which include a protic hydrogen atom and are therefore more polar (a protic hydrogen atom is covalently bonded to a N, O, or F atom and is capable of hydrogen bonding). Furthermore, the examiner agrees with applicant's arguments regarding the rejection over Burnside and Pather, and as such the claims rejected over that rejection have been withdrawn.

Claim 22 is allowed. Claim 22 requires that the particles made have a diameter from 30-100 microns. In contrast, the particles of the prior art reference Kim are sized from 9.5 to 13.2 microns, as of Kim, page 811, abstract. The skilled artisan would not

have been motivated to have increased the size of these particles to have been in the claimed size range.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ISAAC SHOMER/
Examiner, Art Unit 1612

/Frederick Krass/
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